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DISEASES OF THE BILIARY TRACT— CLINICAL AND SURGICAL ASPECTS*

REPORT OF CASE

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IN Hippocrates' writings no mention is made of gall-stones. Galen once observed a large stone which had been passed by rectum. He apparently did not suspect that it came from the biliary tract.

COMMENTS ON LITERATURE

Gentile de Foligno, in 1348, was the first to observe gall-stones. Fernel, in 1554, suggested that gall-stones were the product of thickened bile and that their formation was more likely if one of the biliary ducts became occluded. Johann Fabricus, in 1618, removed a stone from the gall-bladder of a human being. The operation probably was performed on the cadaver.

The seventeenth century marks the beginning of experimental surgery on the gall-bladder. Zambeccari was the first to remove the gall-bladder; he carried out the experiment on a dog. The animal recovered. Michael Entmuller, in 1667, concluded, from experiments by others, that removal of the gall-bladder had no effect on the biliary passages. It was Jean Louis Petit who, in 1743, first operated for the removal of gall-stones. He was of the opinion that before the gall-bladder could be operated on adhesions must first fix the organ to the abdominal wall. Then, by puncturing the gall-bladder through these adhesions, he thought stones could be removed by long forceps. Surgeons of this period were so convinced of the importance of adhesions between the gall-bladder and abdominal wall that substances such as onions and horseradish were applied to the abdomen to bring about this fixation. Later surgeons opened the abdomen and spread these various substances over the parietal peritoneum in order to wall off the gall-bladder. Later others such as Thudicum, in 1859, thought drainage of the gall-bladder should be done in stages; the gall-bladder should first be sutured to the abdominal wall, and it should be opened later.

Bobbs, in 1867, an American surgeon, made the first cholecystostomy. He was of the opinion that he was operating on an ovarian cyst. Marion Sims, in 1878, drained the gall-bladder of a patient who was suffering from dropsy. Death occurred nine days later. In the same year Kocher, Tait, and Keen did this operation with gratifying results. Langenbuch is credited with having done the first cholecystectomy June 15, 1882. The patient's convalescence was without incident. This surgical feat was followed in France by Courvoisier and in America by Ohage in 1887.

Lawson Tait of England was much against removal of the gall-bladder, and apparently for this reason cholecystectomy was not done in that country for several years. Operations on the biliary ducts were first carried out by von Winiwarter, Seyffert, Kümmel, Thornton, Haasler, Kocher, McBurney, and Reidel.

PATHOLOGY

The increase in operations on the gall-bladder has been responsible, naturally, for a large number of injuries to the common bile duct. Most of these accidents have occurred because of technical difficulties encountered at the time of operation. Reconstruction of the common duct has been necessary in many instances in which it has been injured. Pioneers in this type of surgery are Jacobson, W. J. Mayo, Moynihan, and others.

It was once common opinion that if stones could be successfully removed from the gall-bladder, recovery from the symptoms of disease of the gall-bladder inevitably followed. Because of recurrence of symptoms in many of these cases, with or without the formation of additional stones, the gall-bladder itself has received more consideration and the stones less consideration as the probable etiologic factor in the production of that group of symptoms which is believed usually to characterize cholecystitis or cholecystic disease.

Changes in the liver and biliary ducts, associated with certain types of chronic disease of the gall-bladder, have for some time attracted the attention of the surgeon and the pathologist. Some of these changes (hepatitis, cirrhosis) have been so marked as to suggest impairment of certain functions thought normally to be carried on by the liver. These pathologic modifications, then, associated with biliary disease, have stimulated a vast amount of experimental physiologic investigation, not only with regard to the normal function of the liver, but also with regard to the results obtained following experimentally produced lesions that are similar to those frequently seen in certain advanced cases of cholecystitis.

Infection seems to have been considered the greatest single cause of disease of the biliary tracts. Yet, in some instances, it seems fundamentally sound to attribute the etiology to some

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metabolic disturbance. When infection was suggested as the cause of disease of the gall-bladder some discouraging attempts were made to isolate the offending organism. These studies were carried out on cultures made from the bile of grossly diseased gall-bladders. Rosenow, Wilkie, and others, made bacteriologic studies on the wall of the gall-bladder instead of on the bile, and obtained positive cultures in a high percentage of apparently diseased gall-bladders. Wilkie and his coworkers made cultures of gall-bladders removed from patients with clinical histories of cholecystic disease of long standing. Results were positive in 82 per cent of cases. The streptococcus was the predominating organism. In a later, similar group, Wilkie's results were not so encouraging. Concerning those who have been unable to duplicate, to any appreciable extent, Rosenow's and Wilkie's studies, the latter has suggested that the discrepancy was probably due to technical error. He has said that if the mucous membrane is included, when the wall of the gall-bladder is cultured, the small amount of bile adhering to the mucous membrane might be the cause of the negative results. The organisms which have been demonstrated in diseased gall-bladders have been found in the submucous layer and not in the bile or in the mucosa. With regard to infection as the sole cause of cholecystitis, then it may be said that bacteria, or evidence of the presence of bacteria, have not been demonstrated in all cases studied.

TYPES OF CHOLECYSTIC DISEASE

The fact that identical histories characteristic of disease of the gall-bladder can be obtained from patients whose gall-bladders on removal present entirely different pictures, has led to the attempt to classify disease of the gall-bladder. This attempt has not been successful in all respects. For example, the impression may have been gained, from one patient's history, that the gall-bladder contains stones; at operation stones may not be found, and vice versa. Therefore, from clinical or roentgenologic studies, it is not possible to determine definitely in all cases what type of gall-bladder will be found at operation, although in all cases the characteristic subjective and objective features may be the same.

Aschoff many years ago reported peculiar, yellowish, pin-point stippling observed in the mucosa of the gall-bladder in certain cases of clinical cholecystic disease. MacCarty, in 1910, again called attention to such gall-bladders, which W. J. Mayo and Moynihan later described, and which is known now as "strawberry gall-bladder."

Boyd found that this strawberry appearance of the mucous membrane in certain gall-bladders that previously had been described was due to a lipoidal substance, an ester of cholesterol, which filled the cells of the submucosa, protruded into the cells of the mucous membrane of the villi and caused the characteristic strawberry appearance. Mentzer gave the name "cholesterosis" to this condition. One of the reasons suggested for the occurrence of this interesting phenomenon is that the paths of absorption in the submucous layers of the gall-bladder may be blocked, thereby allowing a collection of cholesterol to accumulate in the mucous membrane and that occasionally these fine granules of cholesterol may be shed, forming the nuclei of stones. Occasionally a single cholesterol stone may be found in an otherwise normally functioning gall-bladder, and symptoms of its presence may not occur unless it obstructs the cystic duct. This type of stone is thought to be of metabolic origin, and probably is produced at some such time as the concentration of blood cholesterol is considerably higher than normal. Of one thousand cases of this type, studied by Mentzer and Judd, 60 to 70 per cent of the women dated their first attack at a time during their first pregnancy.

Dewey found, in hypercholesterolized animals, that the lymphatic structures of the gall-bladder were filled with cholesterol. Gosset, Bertrand, and Loewy confirmed this observation. They were of the opinion that the presence of cholesterol in the mucosa, producing the so-called strawberry gall-bladder, was an aseptic process, occurring during a time of hypercholesterolemia, and that infection came secondarily, setting free the cholesterol and causing formation of stones. In half of the one thousand cases of cholesterosis studied by Mentzer and Judd, the gall-bladders contained stones. These authors also observed that in the cases in which stones were present the history was of much longer duration than in those in which stones were absent. It has been suggested that formation of stone in the gall-bladder, which is the site of cholesterosis, may be brought about by the shedding of these bits of cholesterol, forming the nucleus of the stone. It has been observed that if a pure cholesterol stone is dissolved, the nucleus is of an albuminous nature, suggesting the characteristics of a polyp.

Removal of a strawberry gall-bladder, even in the absence of stones, almost invariably gives complete relief, provided the symptoms before operation were those characteristic of cholecystic disease. Not only may negative cultures of the bile and of the wall of the gall-bladder be obtained in this type of disturbance of the gall-bladder, but frequently there is no evidence of infection, such as infiltration of the lymphatic apparatus. In a true sense it would seem that this type of cholecystic disease is of metabolic origin.

In those cases of cholesterosis in which positive cultures of the wall of the gall-bladder, and microscopic evidence of infection can be demonstrated, infection is evidently a secondary factor. Roentgenologic examination of a gall-bladder in which cholesterosis is present is usually negative, regardless of the symptoms, unless sufficient scar tissue is present to prevent absorption of the dye; in that case a positive roentgenologic examination or the presence of a nonfunctioning gall-bladder is reported.

Another type of disturbance of the gall-bladder is clinical cholecystic disease, a term suggested by Judd and McIndoe. Comprising this group are the patients whose histories are typical of disease of the gall-bladder. However, the removed gall-bladder does not contain stones and does not

show evidence, grossly or microscopically, of either an infectious or a metabolic process. The most interesting feature of these cases is that in practically all of them in which pain was the predominating symptom, relief has been obtained by cholecystectomy. Neurosis must be carefully distinguished from this condition. The reason for the symptoms in clinical cholecystic disease is not known. That the sphincter of Oddi loses its power of contraction to a considerable extent following removal of the gall-bladder, allowing a continuous flow of bile into the duodenum, has been demonstrated. It is possible that this phenomenon explains why relief by cholecystectomy is brought about in this type of disturbance of the gall-bladder.

The diffusely infected gall-bladder, with thick, leathery, grayish-white walls, containing many stones, usually is the picture one has in mind when considering cholecystic disease. This process may begin as an inflammatory condition in the wall of the viscus, in the manner in which acute enteritis occurs in typhoid fever. In the acute stage, symptoms of cholecystitis may be present, the process may become chronic and stones may be formed. Another most feasible explanation for this type of cholecystitis is secondary infection superimposed on either of the other two groups just mentioned. It is from this diffusely diseased type of gall-bladder that it is possible to get positive bacterial cultures. The types of stones in this group may be cholesterol and calcium-bilirubin stone, particularly if infection is superimposed on the cholesterosis type of gall-bladder.

In the beginning I mentioned the importance of considering the liver and biliary ducts in connection with cholecystic disease. In removing the gall-bladder a careful examination of the common bile duct is all-important, particularly if the duct is enlarged. The experience of having a patient return several months after cholecystectomy, with the same complaint, and perhaps in addition with jaundice, at once arouses the suspicion that a stone in the common bile duct was overlooked at the time of the first operation. Further surgical interference is, of course, obviously indicated in this type of case. Judd has reported fifty-two cases in this group in which secondary operation revealed a large common bile duct but did not reveal stones. Prolonged external, intermittent drainage, by means of a T tube, effected relief in practically all of the cases; the condition evidently was one of diffuse cholangeitis.

THE HEPATITIS OF CHRONIC GALL-BLADDER DISEASE

Now that I have dealt briefly with certain types of cholecystic disease, with particular reference to the changes found in the gall-bladder, I wish to direct attention to the hepatitis or cirrhosis frequently seen associated with chronic disease of the gall-bladder. Definite, well-defined, and advanced cirrhosis may be present, or there may be mild cirrhosis or hepatitis. Surgical procedures, especially those done on the biliary system in the presence of marked hepatic injury and insufficiency, are carried out with considerable risk.

The studies of Mann and his coworkers on the physiology of the liver, and on the functions of the impaired liver, seem to have some clinical application with reference to hepatic injury resulting from cholecystic disease. It has been demonstrated in the experimental animal that certain changes occur following removal of the normal liver. These changes are as follows: There is marked decrease in the concentration of blood sugar and cessation of formation of urea. Also there accumulates in the tissues of the hepatectomized animal a yellowish pigment which gives a positive reaction for bilirubin. One may say, then, that certain functions of the liver are fairly well defined; the liver has to do with the formation of urea; it is a storehouse for carbohydrates, it maintains a fairly constant level of blood sugar, and it acts as an organ for excretion of bile pigment.

In the experimental animal, very marked cirrhosis can be produced by the frequent administration of carbon tetrachlorid, which has a definitely toxic effect on the liver. If administration of this substance is stopped, rapid regeneration of hepatic substance takes place. Since this result is obtained experimentally by a toxic agent, and since the appearance of the liver compares in every way with that of cirrhosis seen in infection of the biliary tract, as has been mentioned, it seems fair to assume that with infection in the gall-bladder, and particularly in a case with stones in the common bile duct, a definite and constant toxic effect is exerted on the liver. If an animal in which cirrhosis of the liver has been produced by the injection of carbon tetrachlorid is fed the usual diet, consisting largely of proteins, death inevitably occurs in a few days. On the contrary, if a diet of carbohydrate is given, life of the animal is prolonged almost indefinitely. In other words, the injured liver does not tolerate proteins. In an attempt to estimate the value of these experimental results and to determine whether or not they have clinical application, cases of advanced cirrhosis, associated with biliary disease, have been treated preoperatively and postoperatively by means of a diet high in carbohydrate, with very gratifying results, as in the following case:

REPORT OF CASE

A woman, aged fifty-seven years, came to The Mayo Clinic August 28, 1928, complaining of severe attacks of pain in the upper right abdominal quadrant, characteristic of cholecystic disease and of thirty years' duration. Morphin had been necessary for relief. In the ten years previous to her admission at the clinic the attacks had become more frequent and of increased severity. She had been deeply jaundiced for three weeks. There was marked pruritus; the stools had been clay-colored for five weeks. There was a loss of eight pounds in weight. The patient was emaciated. The spleen could be felt about seven centimeters below the costal margin. The edge of the liver scarcely could be felt. There was moderate edema of the ankles. The systolic blood pressure was 170 and the diastolic, 100 millimeters of mercury. The pulse rate each minute was 88 and the temperature 97.6 degrees Fahrenheit. There was a distinct trace of albumin in the urine, and tests for bile were

strongly positive. The Wassermann reaction of the blood was negative. The concentration of blood urea was 64 milligrams in each 100 cubic centimeters. The coagulation time was ten minutes and the calcium time, six minutes. On test of hepatic function, retention of dye was graded three plus. The diagnosis was of chronic disease of the gall-bladder with stones in the common bile duct.

The patient was hospitalized for preoperative treatment. This consisted of a diet high in carbohydrate; 1000 cubic centimeters of a solution which contained ten per cent glucose and one per cent sodium chlorid was given intravenously, daily, and five cubic centimeters of a solution of calcium chlorid ten per cent were given in the vein every other day for six days, that is, three doses in all. At operation the liver was found to be small and high-grade cirrhosis was present. The gall-bladder was conspicuous by being only about 2 by 1.5 centimeters. The common bile duct was enormous and contained many huge stones. After removal of the stones a large T-tube was inserted in the common bile duct for the purpose of external drainage.

The postoperative treatment was similar to that given preoperatively in that large amounts of carbohydrate were given in the form of glucose intravenously, and corn syrup, milk, fruit juices, toast, and so forth, by mouth. The patient's convalescence was uneventful. The jaundice subsided in two weeks. The T-tube was removed on the twenty-first day after operation. The patient was seen two years after operation. She had gained thirty pounds, was of excellent color, and entirely free from symptoms. A test of hepatic function at that time showed only slight retention of dye. The concentration of blood urea was normal.

Comment.—This case is one of many in which this type of treatment has been given. The results are, to say the least, encouraging, and I think they warrant the clinical application of the information that has been obtained as a result of the animal experimental work done as a part of studies on the liver. If three-fourths of a dog's liver is removed, restoration takes place, so that the organ is of normal size in from three to five weeks. The restoration of the liver in the case which I have just cited is evidenced, I think, by the return of hepatic function approximately to normal in a period of less than two years.

CLASSIFICATION OF DISEASES OF THE GALL-BLADDER

The classification of diseases of the gall-bladder which has been used for the last few years is as follows: (1) Acute cholecystitis; (2) chronic cholecystitis, with or without stones; and (3) cholesterosis with or without stones.

Because of the fact that some types of disease of the gall-bladder seem to be of metabolic origin, Judd and McIndoe have suggested the following classification: (1) Acute cholecystitis; (2) metabolic cholecystic disease, with or without stones; and (3) clinical or functional cholecystitis disease.

Acute cholecystitis may have as its cause the organism of typhoid fever. It may occur with, or a number of years following, an attack of typhoid fever. Acute clinical cholecystitis can be produced in the experimental animal by intravenous injection of small amounts of Dakin's solution. The lesion produced in this manner compares favorably with that occasionally found in the clinically diseased gall-bladder. Actually, whether or not clinical cholecystitis occurs in the human being, we do not know. In acute, nonspecific cholecystitis the organisms which are found with great frequency are *Escherichia coli* and *Clostridium welchii*. The condition is usually accompanied by obstruction, which is caused by the impaction of one or more stones in the cystic duct.

In chronic cholecystic disease, bacteria are causal and stones may or may not be present. The condition may be the result of acute cholecystitis or it may come on insidiously. It is from the wall of the gall-bladder in this type of case that Rosenow and Wilkie have isolated the streptococcus.

In metabolic cholecystic disease with or without stones the condition to be met is primarily the so-called strawberry gall-bladder, or cholesterosis. Mentzer, in studying one thousand cases of this type, found that stones were present in 50 per cent. A history of typhoid fever was present in less than 10 per cent of these cases. Cholecystic disease, which frequently occurs during pregnancy, is found to be of this type. It is known that the concentration of blood cholesterol is definitely increased at the time of pregnancy and it seems logical to assume that, at least in certain instances, cholesterosis, or strawberry gall-bladder, is the result. When a single stone is found in this type of gall-bladder it is usually of pure cholesterol. The gall-bladder may be functioning normally, and there may be no symptoms of disease unless the stone obstructs the cystic duct. Infection may invade the strawberry gall-bladder, producing chronic bacterial cholecystic disease with stones, as acute cholecystitis.

Clinical or functional cholecystic disease makes up the third group, which is perhaps the most interesting. Although the symptoms of cholecystitis may be typical, there is little, if any, evidence of disease to be found grossly or microscopically. Yet if the history is typical, relief by removal of the gall-bladder is obtained in a high percentage of cases. Cholecystography has been a great aid in the diagnosis of disease of the gall-bladder. It is a functional test and should be used only to corroborate the clinical observations. If the power of absorption of the gall-bladder has not been interfered with, it can be clearly visualized. Occasionally the roentgenologic report is of a normally functioning gall-bladder, with stones. In all probability, most gall-bladders which contain multiple stones are definitely diseased; their visualization is brought about not because of their ability to absorb the dye, but because of the calcium oxalate in the wall of the gall-bladder. In other words, if a roentgenogram were made without the administration of dye, visualization would be the same. Of the symptoms of disease of the gall-bladder the most characteristic is pain. If this is present, regardless of the type of gall-bladder, cholecystectomy gives permanent relief in a vast majority of cases.

Cholangeitis may produce the symptoms of stones in the common bile duct. Treatment by external biliary drainage, using a T-tube, brings relief in the majority of cases.

Experimental physiologic investigation seems to have definite clinical application in that the preoperative and postoperative treatment in cases of hepatic cirrhosis complicating disease of the gall-bladder is best treated by feedings high in carbohydrate and low in protein.

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RESPIRATORY FAILURE IN POLIOMYELITIS—ITS TREATMENT WITH THE DRINKER RESPIRATOR*

REPORT OF CASES

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DRINKER[1] first described the construction and operation of his mechanical respirator in May 1929, and since that time there have been reported in the literature five cases[2,3,4] of respiratory failure due to poliomyelitis treated in the respirator. Several other cases were mentioned but not reported in detail. A Drinker respirator was installed in the Communicable Disease Department of the Children's Hospital, San Francisco, in August 1930, and a second machine the latter part of October 1930. Since the installation of the first respirator fifteen patients with varying degrees of respiratory involvement due to poliomyelitis have been treated in these machines. Most of these were in urgent need of artificial respiration and could not have survived long without some form of assistance. A few patients were in less desperate condition, but treatment in the respirator was used to relieve them of fatigue and anxiety, to secure rest for the involved muscles of respiration and, as they improved, to increase chest expansion.

Nine of our patients had respiratory difficulty due to intercostal weakness or paralysis; three of these patients died. One patient had chiefly diaphragmatic involvement and is apparently recovering. Five of the patients showed bulbar involvement and none of these survived.

The type of respiratory failure most favorable for treatment in the respirator is that due to intercostal paralysis. These patients, if left alone, may die early of asphyxia or later of pneumonia secondary to atelectasis. The diagnosis of intercostal paralysis is not difficult. In our series intercostal paralysis was constantly associated with paralysis of the muscles of the shoulder girdle on one or both sides, and frequently disappearance of the upper abdominal reflexes was noted just before intercostal weakness was first apparent. These patients show moderate increase in respiratory rate and the respirations are shallow, frequently asymmetrical and effected chiefly by the diaphragm. As the condition progresses, paradoxical respiration is noted in which the upper chest collapses synchronously with inspiratory effort of the diaphragm and rises during the act of expiration. This is, of course, due to failure of the upper intercostals to help in respiration and to their inability to maintain expansion of the upper chest cage against pull of the diaphragm. As a result there is very poor pulmonary ventilation, necessitating constantly increasing effort on the part of the diaphragm which leads to progressive fatigue of the diaphragm and finally respiration ceases. Sometimes the onset of diaphragmatic exhaustion is extremely abrupt.

The response of these patients to the respirator was very gratifying. Usually before their condition became alarming they were told that if they became too fatigued they could have the help of the respirator, and in several instances patients asked to be placed in the machine for a trial. A few of the children were very apprehensive and had to be given opiates over a short period when first placed in the respirator. None of these patients had any difficulty in adapting themselves to the rhythm of the machine. Brief case histories follow.

REPORT OF CASES

CASE 1.—A male adult of thirty-one years was transferred to the Children's Hospital from the San Francisco Isolation Hospital on August 17, 1930, the sixth day of his illness. He had at that time, in addition to complete intercostal paralysis, almost complete paralysis of both lower extremities and of the right shoulder, marked weakness of the abdominal muscles and urinary retention. He was extremely apprehensive and his condition appeared desperate. His breathing was entirely diaphragmatic, there were fibrillary tremors of the neck muscles, there was moderate cyanosis and the pulse was weak and irregular. The respirator immediately relieved the patient's distress, and the improvement in his condition was striking. He was kept in the machine almost continuously for one week, then was kept out for increasingly longer periods until the sixteenth day after entry, when he was able to remain out.

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CASE 2.—A woman of thirty-five years, who entered with complete flaccid paralysis of both upper and lower extremities and left facial weakness, developed some evidence of intercostal weakness on August 16, 1930, but without cyanosis or any change in the pulse. On August 20, 1930, about midnight her respiration failed quite suddenly, apparently due to exhaustion of the diaphragm. She was comatose and extremely cyanotic and respiratory effort had practically ceased. The respirator was occupied at the time by Case 1, but it was possible to remove him for a time and this patient was placed in the respirator and kept there about ten hours. Her improvement was prompt. At the end of ten hours, however, the first patient's condition was so much worse that return to the respirator was imperative. The second patient was given artificial respiration manually together with oxygen throughout the afternoon and evening, despite which death occurred at 11:55 p. m. August 20, 1930. This patient's improvement while in the respirator was such that it seemed she might have survived if it had been possible to continue treatment in the machine. At autopsy the destructive lesions found in the cord were so complete and extensive that return of function would have been doubtful.

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Editor's Note: Description of the Drinker Respirator by the American Medical Association Council on Physical Therapy is given in the "Journal of the American Medical Association," May 9, 1931, page 1580.